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Case Report

Bronchial atypical carcinoid tumor without invasion but with marked intraluminal growth like branchial tree cast

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ABSTRACT

Pulmonary carcinoid tends to show intraluminal growth. However, pulmonary atypical carcinoid showing bronchial tree-like cast is extremely rare. A 63-year-old man was admitted to our hospital because of cough and sputum. Imaging modalities including XP, US, CT, and MRI showed bronchial tree-like tumor shadow in the right middle and lower lobes. Transbronchial biopsy revealed atypical carcinoid. A lobectomy of the right middle and lower lobe and lymph node dissection were performed. Grossly, the resected specimens showed cast-like tumor within the bronchial tree. It contained necrotic areas. Microscopically, the tumor cells were arranged in trabecular, ribbon, and insular patterns. There were many necrotic areas. The tumor cells showed hyperchromatic nuclei, and mitotic figures were recognized in 4 per 2 mm^2. Parenchymal invasion was not recognized. Lymphovascular permeation was absent. Immunohistochemically, the tumor cells were positive for cytokeratins, synaptophysin, chromogranin, CD56, and neuron-specific enolase, but negative for S100 protein, melanosome, p53 protein, and KIT. The Ki-67 labeling was 15%. The tumor cells were stained with Grimelius stains. The lymph nodes showed no metastatic lesions. Therefore, atypical carcinoid was diagnosed. The patient was followed up with adjuvant chemotherapy, and is now alive free from tumor 7 years after the operation. In summary, clinicians and pathologists should be aware that atypical carcinoid can show branchial tree-like casts within the bronchial lumens but without parenchyma invasion. Such atypical carcinoids may have favorable prognosis.

1. Introduction

Pulmonary carcinoid is an uncommon tumor in the lung. According to WHO blue book,[1] carcinoid tumors are characterized by growth patterns (organoid, trabecular, insular, palisading, ribbon, rosette-like arrangements) that suggest neuroendocrine differentiation. Tumor cells have uniform cytoplasmic features with moderate eosinophilic, finely granular cytoplasm, and nuclei with a finely granular chromatin pattern.[1] Carcinoid tumor is classified into typical and atypical ones, depending on the mitotic activity and the presence of necrosis.[1] Typical carcinoid is defined as a carcinoid tumor with fewer than 2 mitoses per 2 $mm^2$and lacking necrosis.[1] In contrast, atypical carcinoid is defined as a carcinoid tumor with 2–10 mitoses per 2 mm^2 and/or foci of necrosis.[1] The 2 mm^2 corresponds to 10 high power fields of the light microscopy.[1]

Carcinoid tumors tend to show intraluminal growth.[1–4] However, carcinoid entirely composed of intrabranchial elements with features of bronchial tree cast is extremely rare. Here, the author presents a surgical case of atypical carcinoid with this intrabranchial tree cast-like features without invasion.

2. Case report

A 63-year-old man presented with longstanding cough and sputum and was admitted to our hospital for scrutiny. A blood laboratory test showed mild anemia and tumor markers were within normal ranges. However, imaging modalities including chest-XP, US, CT, and MRI revealed a bronchial tree-like tumor shadow in the right middle and lower lobes. A transbronchial biopsy was obtained, and it was diagnosed as an atypical carcinoid by the author. Therefore, a lobectomy of the right middle and lower lobe and lymph node dissection were performed. Gross findings were very impressive. Grossly, the resected specimens showed cast-like tumor in most of the bronchial tree (Fig. 1A and B). It contained necrotic areas. No invasive features were recognized. Thirty-eight sections were examined for histology. Microscopically, the tumor cells were consisted of monotonous cells with relatively monotonous hyperchromatic nuclei and monotonous acidophilic cytoplasm (Fig. 2), Tumor cells were arranged in trabecular, ribbon-

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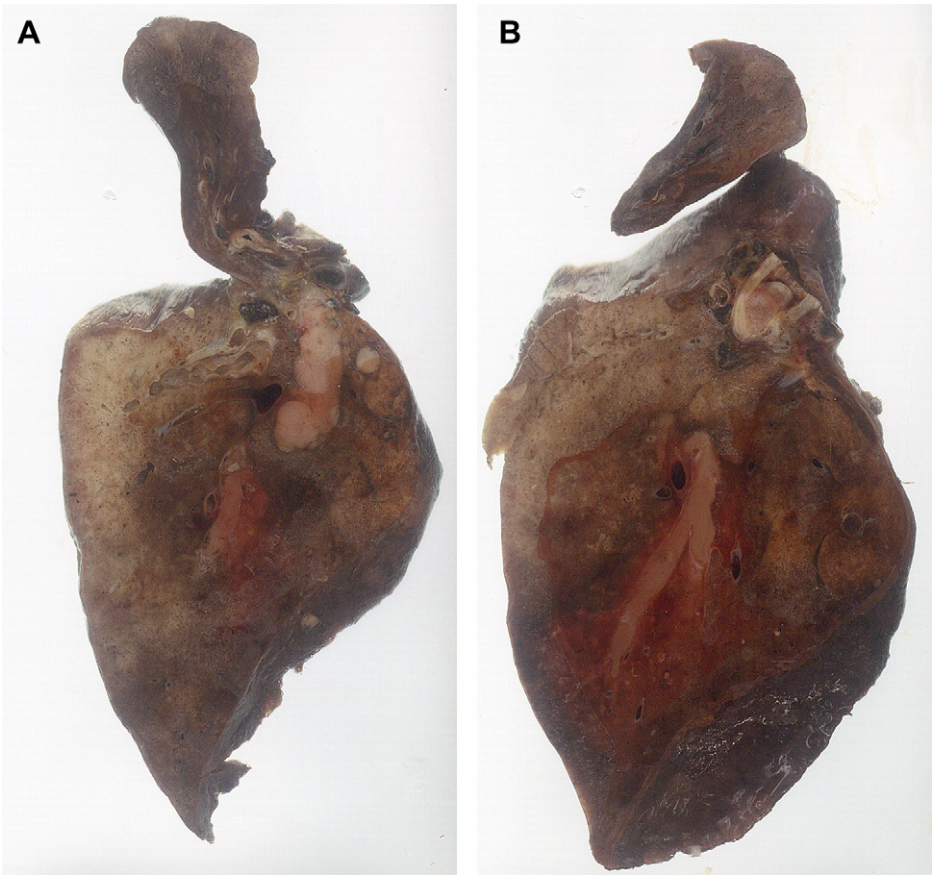

Fig. 1. A and B: cut surface of the lung. A bronchial tree-like tumor is seen, as if it is a bronchial tree cast. The tumor is totally within the branchial lumens.

like, and insular patterns (Fig. 2). There were many necrotic areas (Fig. 3). Mitotic figures were recognized in 4 per 2 mm^2 (10 high power fields). No lymphovascular permeation was recognized. Parenchymal invasions were absent, but the tumor was pushing the parenchyma (Fig. 4). The bronchial surgical margin was negative. The pleura was not involved by tumor cells. Therefore, the author thought that the tumor was completely removed and the prognosis will be relatively good. The mucus impactions were recognized in the periphery of the intrabronchial atypical carcinoma, but they were scant in amount. The lung parenchyma showed obstructive bronchopneumonia.

An immunohistochemical analysis was performed with the use of Dako Envision method (Dako, Glostrup, Denmark), as described previously.[5,6] No melanin pigment was recognized by HE and Masson-Fontana stains Tumor cells were positively labeled with Grimelius stain. Immunohistochemically, the tumor cells were

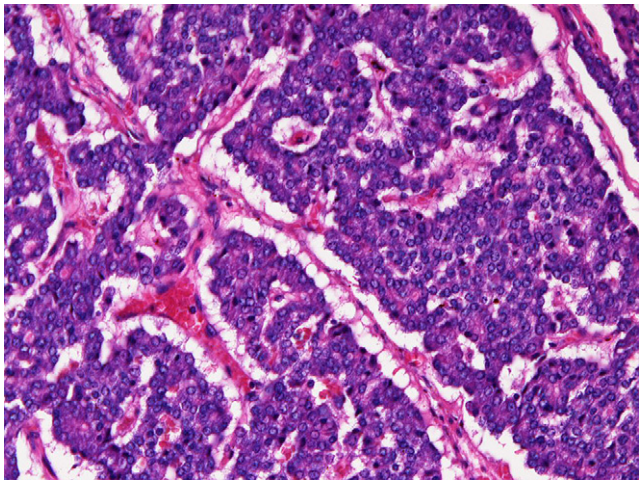

Fig. 2. Microscopic findings. The tumor cells show neuroendocrine features such as ribbon, trabecular, and insular patterns. The tumor cells are relatively monotonous. HE, ×200.

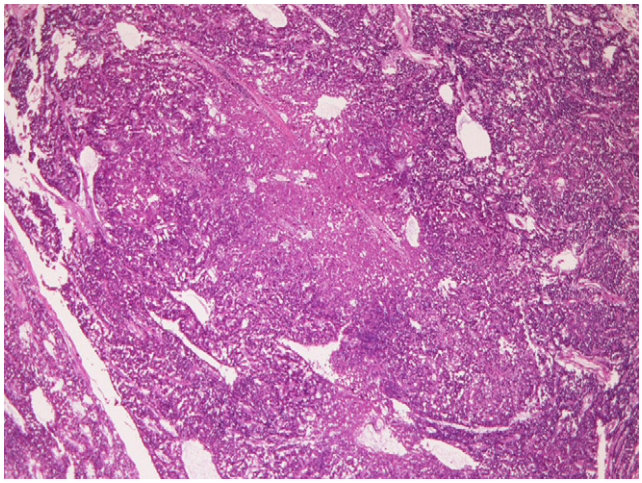

Fig. 3. There is a necrotic foci with the atypical carcinoid, ×200.

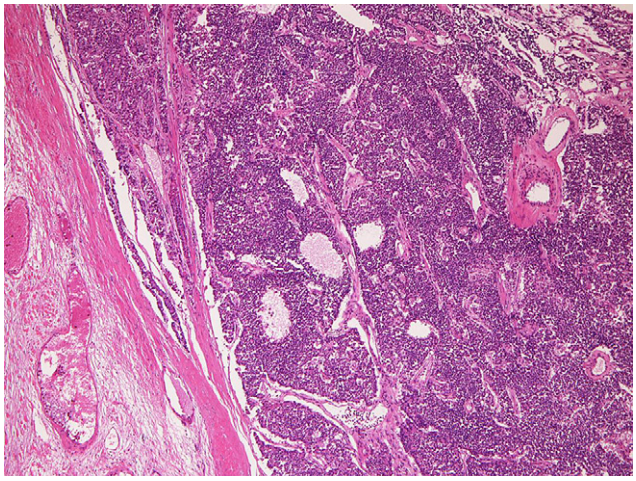

Fig. 4. The carcinoid tumor within the peripheral bronchus. The tumor is located within the bronchi, pissing lung parenchyma. No invasion is seen. HE, ×200.

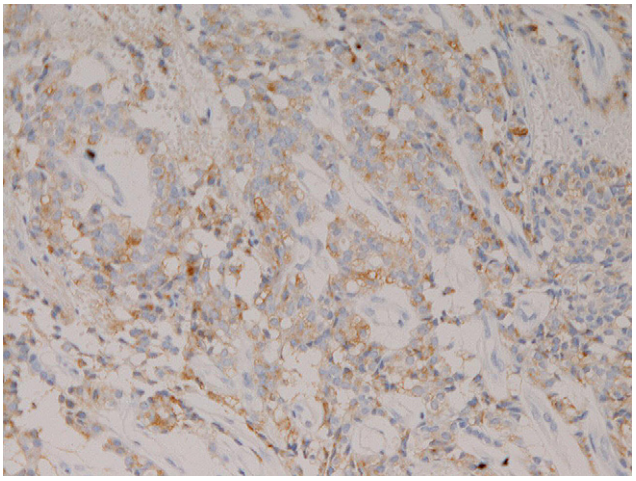

Fig. 6. The tumor cells are positive for chromogranin, ×200.

positive for cytokeratin (Fig. 5) (AE1/3, Dako; CAM5.2, polyclonal wide, Dako, Beckton-Dickinson, CA, USA), chromogranin (Fig. 6) (DAK-A3, Dako), synaptophysin (polyclonal, Dako), neuron-specific enolase (BBS/NC/VI-H14, Dako), CD56 (MOC-1, Dako), and PDGFRA (Santa Cruz, CA, USA). In contrast, the tumor cells were negative for S100 protein, vimentin (Vim 3B4, Dako), melanosome (HMB45, Dako), p53 protein (DO-7, Dako), CD34 (QBEND10, Dako), desmin (D33, Dako), α-smooth muscle actin (1A4), KIT (polyclonal, Dako), CD3 (M7193, Dako), CD79α (M7050, Dako), and CD20 (L26, Dako). Ki-67 labeling (MIB1, Dako) was 15%. The lymph nodes ($n = 15$) showed no metastatic lesions. Therefore, atypical carcinoid was diagnosed. The patient was followed up with adjuvant chemotherapy, and is now alive free from tumor 7 years after the operation.

3. Discussion

Pulmonary neuroendocrine tumors were classified into typical carcinoid, atypical carcinoid, large cell neuroendocrine carcinoma (LCNEC), and small cell lung carcinoma (SCLC).[7] These tumors were characterized by neuroendocrine features, which indicate positive neuroendocrine antigens including CD56, chromogranin, synaptophysin and neuron-specific enolase as well as positive neuroendocrine granules detected by ultrastructural observations.[1,7,8] Tumor of the present case was immunohistochemically positive for these neuroendocrine antigens. Thus, the present tumor is pulmonary neuroendocrine tumor. The histologies also indicate that the tumor of the present case is a neuroendocrine tumor.

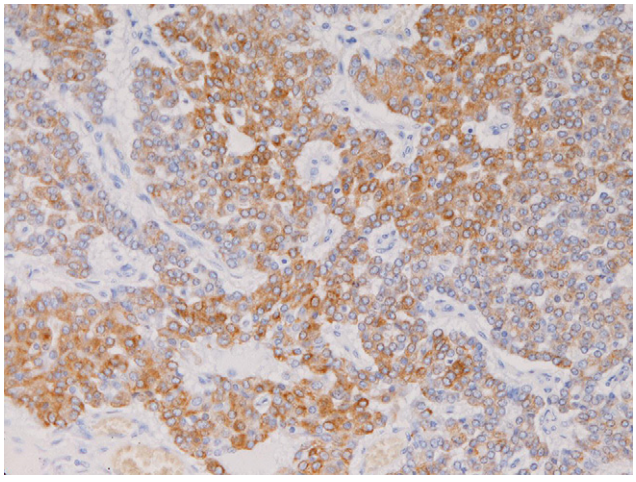

Fig. 5. The tumor cells are positive for cytokeratin, ×200.

These pulmonary neuroendocrine tumors have different morphologies and biological behaviors. Typical and atypical carcinoids show ribbon-like, trabecular, sinusoidal, insular, and organoid pattern.[1] The tumor cells were monotonous and do not show apparent malignant features.[1] Typical carcinoid is potentially malignant, whose malignant potential depends on tumor size and cellular atypia. Atypical carcinoma is low grade malignant tumor, and also called malignant carcinoid. The differentiation between typical and atypical carcinoids depends on mitotic activity and necrosis.[1,7–9] The histology of LCNEC is that of large cell carcinoma. Of large cell carcinoma, the tumors with neuroendocrine features are called LCNEC. LCNEC is an aggressive tumor. SCLC is cytologically characterized by small cells with hyperchromatic nuclei, negative nucleoli, nuclear molding, numerous mitoses, and scant cytoplasm. SCLC does not show carcinoid-like histological features such as ribbon and trabecular features. SCLC is highly aggressive tumor. Therefore, the tumor of the present case is an atypical carcinoid.

The origin of these neuroendocrine tumors is considered to be endocrine cells present in the bronchus or Kulchitsky cells or APUD cells.[10–12] These cells are often seen in fetal bronchi and are believed to be of endodermal origin.[10,11] In the present case, the only involved organ is bronchus. The observations suggest that endocrine cells normally present in the bronchial epithelium undergo tumor formation, thus leading to the atypical carcinoid within the bronchial lumens.

Very interestingly, the tumor of the present case showed macroscopical features of bronchial tree-like casts. Carcinoid tumor of the lung occasionally show intrabronchial polyp.[1–4] However, the bronchial tree-like cast as seen in the present study is very rare, and the author cannot find such a case in the English literature. Microscopical examination also indicated that the tumor of the present case were totally located in the bronchial lumen, without lung parenchymal invasion or involvement. The intrabronchial growth reflects that the intrabronchial space is free of resistance for cancer invasion. The negative parenchymal invasion in the present case suggests that the invasive biological behavior is lacking or very little in the present study. The absence of lymphovascular permeation of the present case shows no aggressive biological behavior. These benign biological behaviors may be associated with presence

of cell adhesion molecules such as the cadherin-catenin system,[13,14] and lack of many molecules involved in tumor cell invasion, including matrix metalloproteinases.[15]

The prognosis of atypical carcinoid is relatively poor. The 5- and 10-year survival was 56 and 35%, respectively.[7] Other studies showed 69 and 59%, respectively,[8] and still others 77 and 53%, respectively.[9] In the present case, the surgical margin was negative and the tumor did not involve the pleura. In addition, there was no lymphovascular permeation. The author thought that the tumor was totally resected, and anticipated that the prognosis is relatively good. In fact, the patient is now healthy without recurrence and metastasis seven years after the operation.

In summary, clinicians and pathologists should be aware that atypical carcinoid can show bronchial tree-like casts within bronchial lumens without parenchyma invasion. Such atypical carcinoids may have favorable prognosis.

Conflict of interest

The author has no conflict of interest.

References

1. Beasley MB, Geisinger K, Thunneissen FB, et al. Carcinoid tumour. In: Travis WD, Blambillia E, Muller-Hermelink K, Harris CC, editors. *World Health Organization classification of tumours. Pathology and genetics of tumours of the lung, pleura and heart*. Ryon: IARC Press; 2004. p. 59–62.
2. Van Boxem TJ, Golding RP, Venmans BJ, Postmus PE, Sutedja TG. High-resolution CT in patients with intraluminal typical carcinoid tumors treated with bronchoscopic therapy. *Chest* 2000;**117**:125–8.
3. Sutedja TG, Schreurs AJ, Vanderschueren RG, Kwa B, vd WElf TS, Portmus PE. Bronchoscopic therapy in patients with intraluminal typical bronchial carcinoid. *Chest* 1995;**107**:556–68.
4. Brokx HA, Risse EK, Paul MA, Grunbern K, Golding RP, Kunst PW, et al. Initial chronchoscopic treatment for patients with intraluminal chronchial carcinoids. *J Thrac Cardiovas Surg* 2007;**133**:973–8.
5. Terada T, Kawaguchi M, Furukawa K, Sekido Y, Osamura Y. Minute mixed ductal-endocrine carcinoma of the pancreas with predominant intraductal growth. *Pathol Int* 2002;**52**:740–6.
6. Terada T, Kawaguchi M. Primary clear cell adenocarcinoma of the peritoneum. *Tohoku J Exp Med* 2005;**271**:271–5.
7. Travis WD, Rush W, Flieder DB, Falk R, Fleming MV, Gal AA, et al. Survival analysis of 200 pulmonary neuroendocrine tumors with classification of criteria for atypical carcinoid and its separation from typical carcinoid. *Am J Surg Pathol* 1998;**22**:934–44.
8. Soga J, Yakuwa Y. Bronchopulmonary carcinoids: an analysis of 1,875 reported cases with special references to the comparison between typical carcinoids and atypical varieties. *Ann Thrac Cardiovasc Surg* 1999;**5**:211–9.
9. Olliaro A, Filosso PL, Donati G, Ruffini E. Atypical bronchial carcinoid: review of 46 patients. *J Cardiovas Surg* 2000;**41**:131–5.
10. Gould VE, Linnnoila RI, Memoli VA, Warren WH. Neuroendocrine components of the bronchopulmonary tract: hyperplasia, dysplasia, and neoplasms. *Lab Invest* 1983;**49**:519–37.
11. Sidhu G. The endodermal origin of digestive and respiratory tract APUD cells: histopathologic evidence and a review of the literature. *Am J Pathol* 1979;**96**: 5–20.
12. Salyer DC, Salyer WR, Eggleston JC. Bronchial carcinoid tumors. *Cancer* 1975;**36**:1522–37.
13. Endo K, Ohta T, Terada T. Immunoreactive E-cadherin, alpha-catenin, beta-catenin and gamma-catenin proteins in hepatocellular carcinoma: relationships with tumor grade, clinicopathologic parameters and patients' survival. *Hum Pathol* 2000;**31**:558–65.
14. Terada T, Ashida K, Kitamura Y, Matsunaga Y, Takashima K, Kato M, et al. Expression of E-cadherin, alpha-catenin and beta-catenin during human intrahepatic bile duct development. *J Hepatol* 1998;**28**:263–9.
15. Terada T, Okada Y, Nakanuma Y. Expression of immunoreactive matrix metalloproteinases and tissue inhibitors of matrix metalloproteinases in human normal livers and primary liver tumors. *Hepatology* 1996;**23**:1341–4.